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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,302	07/26/2006	Chi Vu	B2047-7033US	1885

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EXAMINER	
KIFLE, BRUCK	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
05/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/552,302	VU ET AL.	
	Examiner	Art Unit	
	Bruck Kifle	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/29/2009 has been entered.

Claim Rejections - 35 USC § 112

Claims 1-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In the definition of the linkers of "L" it is unclear what the point of attachment to X^1 is and which side is connected to X^2. A clarification is required.

ii) In the definition of R' and R" the term "acyl" is present. It is unclear what this group looks like. Is this an alkanoyl, the group R-C(O), wherein R is alkyl (i.e., acyl of a carboxylic acid) or are acyls of other acids (such as arsenic, phosphonic, etc.) also intended? A clarification is required.

iii) In claims 8, 9, 19, 20, 21, 28-46 there are substituents on the R^1 group. No substituents are allowed on the R^1 groups in claim 1. These claims, however, have substituents that are neither present nor permitted in claim 1. The claims lack antecedent basis in claim 1.

iv) In claim 22 there is a period after "22." Deletion is required.

Claims 35-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding claims 35, 36, 39 and 40, the how to use portion of the statute has not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what disease and what symptoms are to be treated. In this case, Applicants have not provided what is being treated by these claims, who the subject is, how one can identify said subject (i.e. how one can identify a subject in need), given no specific dose, given no specific dosing regimen, given no specific route of administration, and do not specify what diseases or symptom they intend to treat.

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001.

Claims 37 and 38 read on inhibiting the A_{2a} adenosine receptor *in vitro*, inhibiting the A_{2a} adenosine receptor in mammals with below normal A_{2a} adenosine receptor activity, inhibiting the A_{2a} adenosine receptor in mammals with normal A_{2a} adenosine receptor activity, or in asymptomatic mammals with up-regulated A_{2a} adenosine receptor activity. The specification fails to teach any benefit to be gained from such actions. Is extensive experimentation required on the part of a potential infringer to determine if his

use of Applicants' inhibitor falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967).

As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

Regarding claims 41-46, Applicants appear to rely on the compounds ability to inhibit the A_{2a} adenosine receptor to treat and prevent a disease or disorder selected from the group consisting of Parkinson's disease, progressive supranuclear palsy, multiple system atrophy, Alzheimer's disease, depression, AIDS encephalopathy, multiple sclerosis, amyotrophic lateral sclerosis, migraine, attention deficit disorder, narcolepsy, sleep apnea that results in excessive daytime sleepiness, Huntington's disease, cerebral ischemia, brain trauma, hepatic fibrosis, cirrhosis, and fatty liver.

These claims are considered reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general

format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition or modulation of adenosine A_{2a} receptors by the instant compounds, instant claims reaches through treating and preventing any or all diseases and disorders stated above in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor or modulator of adenosine A_{2a} receptors, based on limited assay, it is claimed that treating and preventing all diseases or disorders stated above, for which there is no enabling disclosure.

The scope of the claims is not adequately enabled solely based on the activity of the compounds to inhibit or modulate the adenosine A_{2a} receptor for which applicants provide no competent evidence. Many if not most of central nervous system diseases such as Alzheimer's disease, ALS, multiple sclerosis etc. are very difficult to treat. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease despite the fact that there are many drugs, which can be used for "inflammatory condition".

That a single class of compounds can be used to treat all diseases and disorders stated above in general embraced in the claims is an incredible finding for which applicants have not provided supporting evidence.

Even a recent review of adenosine receptors suggest the use of these antagonists still under experimental stage and speculative in nature. See Baraldi et al., European Journal of Medicinal Chemistry 38: 367-382, 2003.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The state of the art is indicative of the requirement for undue experimentation.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating various central nervous diseases that require adenosine A_{2a} inhibitory or modulatory activity.

2) The state of the prior art: A very recent publication expressed that the effects of adenosine A_{2a} inhibitory activity is still in experimental stage and is unpredictable. See Baraldi et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the treatment of all diseases and disorders stated above by the instant compounds.

Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show all diseases or disorders stated above can be treated based on the test results of adenosine A_{2a} inhibitory activity and the state of the art is that the effects of adenosine receptor antagonists are unpredictable.

6) The breadth of the claims: The instant claims as recited embrace treatment of various diseases and disorders.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention

Several requests were made to Applicants to point to the excluded compounds in the prior art but Applicants have so far refused to do so pointing instead that these compounds are present in the prior art of record. A complete response would be considered pointing to the actual reference and pointing out by page and line number (or example number as appropriate) where these compounds are disclosed. Thousands of pages are present in the about 170 references cited.

The disclosure of these prior art compounds are material to the examination of the instant application.

This would be the final attempt from the examiner that Applicants comply with the examiner's request to point to the compounds excluded by proviso since these compounds were excluded to avoid prior art rejections. Further refusal by Applicants would be referred to management for appropriate action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is 571-272-0668. The examiner can normally be reached on Mondays-Fridays from 8:30 AM -6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruck Kifle/
Primary Examiner
Art Unit 1624

May 6, 2010